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(54) Mass spectrometry of solution and apparatus therefor

Massenspektrometrie von Lösungen und Vorrichtung dafür

Spectrométric de masse pour des solutions et dispositif associé

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- **PATENT ABSTRACTS OF JAPAN vol. 009 no. 220 (E-341) ,6 September 1985 & JP-A-60 079656 (HITACHI SEISAKUSHO KK) 7 May 1985,**
- **JOURNAL OF PHYSICS D. APPLIED PHYSICS, vol. 25, no. 5, 14 May 1992 pages 761-773, XP 000304739 SAUERS I ET AL 'A MASS SPECTROMETRIC STUDY OF POSITIVE AND NEGATIVE ION FORMATION IN AN SF6 CORONA PART I: SOURCES OF SULPHUR-FLUORIDE IONS'**
- **TRAC, TRENDS IN ANALYTICAL CHEMISTRY, vol. 13, no. 2, 1 February 1994 pages 81-90, XP 000425825 BRUINS A P 'ATMOSPHERIC-PRESSURE-IONIZATION MASS SPECTROMETRY II. APPLICATIONS IN PHARMACY BIOCHEMISTRY AND GENERAL CHEMISTRY'**
- **PATENT ABSTRACTS OF JAPAN vol. 018 no. 373 (P-1769) ,13 July 1994 & JP-A-06 102246 (HITACHI LTD) 15 April 1994,**

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Description

BACKGROUND OF THE INVENTION

[0001] The present invention relates to a mass spectrometry of a solution and particularly to a mass spectrometer for analyzing substances in a solution and an apparatus for combining a liquid chromatograph used for separation and analysis of a mixed sample and the mass spectrometer.

[0002] At present, development of a mass spectrometry of biological substances is regarded as important in the field of analysis. Biological substances are generally dissolved in a solution as a mixture, so that an apparatus for combining a means for separating a mixture and a mass spectrometer is under development. As a typical apparatus of this method, there is a liquid chromatograph - mass spectrometer (hereinafter abbreviated to LC/MS) available. A liquid chromatograph (hereinafter abbreviated to LC) is superior in separation of a mixture but cannot identify each substance, whereas a mass spectrometer (hereinafter abbreviated to MS) is highly sensitive and superior in identification ability but not suitable to analysis of a mixture. Therefore, an LC/MS using an MS as an LC detector is very useful in analysis of a mixture.

[0003] The LC/MS using the conventional atmospheric pressure chemical ionization method which is disclosed in Japanese Patent Application Laid-Open 5-325882 will be explained hereunder by referring to Fig. 9.

[0004] A sample solution eluted from a liquid chromatograph 14 is introduced into a metallic tube 3 via a pipe 1 and a connector 2. The sample solution comprises a sample and a mobile phase (a buffer solution which flows into the separation column when the sample is separated in the LC). However, for the purpose of improving the ionization efficiency in the ion source (according to the present invention, it means a portion for converting a substance to be analyzed existing in the liquid phase to ions in the gas phase and includes a spray portion for spraying a solution, a vaporization portion for vaporizing droplets generated by the spray portion, and an ionization portion for ionizing a substance), a solvent different from the mobile phase may be added. The metallic tube 3 is embedded in a metallic block 4a. When the metallic block 4a is heated by a heating means such a heater, a sample solution introduced in the metallic tube 3 is sprayed. Fine droplets generated by spraying are introduced and vaporized in the vaporization portion 5 comprising a heated metallic block 4b. Sample molecules vaporized in the vaporization portion 5 are introduced into the ionization portion 6. A needle electrode 7 is installed in the ionization portion 6. When a high voltage is applied to this needle electrode 7 from a high voltage source 8a, a corona discharge is generated in the ionization portion 6.

[0005] Assuming A as sample molecules to be analyzed and B as molecules of reaction gas, the atmospheric pressure chemical ionization method is a method for ionizing A by a chemical reaction of A and B. As a typical ion chemical reaction, there are a protonation reaction and a deprotonation reaction available as shown below.

$$A + BH^+ \rightarrow AH+ + B \qquad \text{(Protonation reaction)}$$

$$A + B^- \rightarrow (A - H)^{\cdot} + BH \qquad \text{(Deprotonation reaction)}$$

[0006] According to the prior art shown in Fig. 9, hydronium ions (H_3O+) are generated when a corona discharge is generated in the atmosphere and ions AH+ of the sample A are generated by using the following reaction between the hydronium ions and the sample molecules A.

$$A + H_3O^+ \rightarrow AH^+ + H_2O$$

[0007] Ions of the sample generated by chemical ionization in the ionization portion 6 are deflected in trajectory by a voltage applied to a deflection electrode 31 by a power source 30 and drifted toward an ion introduction aperture 9a. The ions fetched by the ion introduction aperture 9a are introduced into a high vacuum portion 12 which is exhausted in a high vacuum by an exhaust system 10b via a differential pumping portion 11 which is evacuated by an exhaust system 10a and an ion introduction aperture 9b. When ions and solvent molecules are fetched from the ion introduction apertures 9a and 9b, they are cooled by adiabatic expansion, so that so-called clustering for condensing the ions and solvent molecules again is caused. To prevent the clustering, the electrodes having the ion introduction apertures 9a and 9b are heated. The mass of ions introduced into the vacuum is analyzed by a mass spectrometric portion 13. Nonvolatile compounds that are not ionized in the ionization portion 6 are diffused in the atmosphere and captured by a capture plate 32.

[0008] An LC/MS using the conventional electrospray method which is disclosed in Japanese Patent Application Laid-Open 6-102246 will be explained by referring to Fig. 10. A sample solution eluted from the LC is introduced in the metallic tube 3 via the pipe 1 and the connector 2. A high voltage is applied between the metallic tube 3 and an electrode 21c having the ion introduction aperture 9a by using a high voltage source 8b and the sample solution is electrostatically sprayed. To assist electrospray, gas such as nitrogen gas is let flow from a spray gas outlet 40. When fine charged droplets generated by electrospray are vaporized, gaseous ions are generated. However, the diameter of droplets at the center of the jet is large and it is difficult to vaporize droplets with a large diameter, and furthermore when drop-

lets with a large diameter are adhered to the electrode 21c, the temperature of the electrode 21c lowers and the ion intensity obtained in the mass spectrometric portion may vary. Therefore, a shielding plate 41 for shielding the center of the jet is installed between the metallic tube 3 and the electrode 21c and the outer periphery of the jet is sprayed toward the ion introduction aperture 9a. Generated ions are introduced into the high vacuum portion 12 via the ion introduction aperture 9a, the differential pumping portion 11, and the ion introduction aperture 9b and analyzed by the mass spectrometer installed in the high vacuum portion 12.

[0009] For analysis of biological substances and environmental contaminants, a method for analyzing a sample solution containing nonvolatile compounds of high concentration is required.

[0010] For example, in the LC, the mobile phase including a nonvolatile salt is often used experientially so as to enhance the separation ability and the reproducibility of the retention time. As a result, a method for analyzing a sample solution containing a nonvolatile salt is desirable for a detector of the LC.

[0011] Nonvolatile compounds are contained in not only samples obtained from a living matter such as urine, perspiration, and blood but also samples relating to the environment such as effluents from a factory and water of a lake or marsh. To remove nonvolatile compounds from these collected samples, a complicated pretreatment such as desalting is required. Therefore, to analyze biological substances and environment contaminants briefly, a method for analyzing a sample solution containing nonvolatile compounds is required.

[0012] However, in a mass spectrometric apparatus using the conventional atmospheric pressure chemical ionization method show in Fig. 9, when a sample solution containing nonvolatile compounds of high concentration is introduced into the ion source of the mass spectrometric apparatus comprising an ion source, a differential pumping portion, and a mass spectrometric portion, a problem arises that ions of a substance to be analyzed cannot be analyzed stably for many hours. The reason is that since the sample solution is sprayed by using the heated metallic tube, solvent molecules are vaporized in the tube and nonvolatile compounds are salted out on the inner wall of the tube. The inner diameter of the metallic tube becomes smaller because nonvolatile compounds are salted out on the tube wall and the metallic tube clogs up finally. Therefore, the spray status varies with time, so that the ion generation in the ionization portion is adversely affected.

[0013] When fine droplets containing nonvolatile compounds are adhered to the neighborhood of the ion introduction aperture installed between the ion source and the differential pumping portion, solvent molecules are vaporized and nonvolatile compounds are salted out around the aperture. In the conventional apparatus shown in Fig. 9, by installing the capture plate on the ion side, a method for salting out nonvolatile compounds contained in droplets adhered to the capture plate on the capture plate is used so as to reduce salting out of nonvolatile compounds around the aperture. However, it is actually difficult to capture all droplets sprayed in the atmosphere on the capture plate and a part of droplets is diffused in the atmosphere and reaches around the aperture. Therefore, if the analysis is continued for many hours, an actual problem arises that salted nonvolatile compounds clog up the aperture and ions cannot be fetched by the mass spectrometric portion.

[0014] As an example of a sample solution containing nonvolatile compounds, a case that a sodium phosphate water solution having a concentration of 20 millimol/liter (hereinafter described as a phosphoric acid buffer) is introduced into the ion source at a flow rate of 50 micro liter per minute will be described hereunder. A phosphoric acid buffer is a mobile phase which is often used in a detector other than the MS, for example, an LC having an ultraviolet absorption detector. When a conventional LC/MS uses a phosphoric acid buffer, the observed ion intensity starts lowering within about 30 minutes after start of analysis and lowers down to about 1/10 when one hour elapses, and the continuation of analysis becomes difficult.

[0015] Whether a problem that the metallic tube or aperture clogs up due to salting out of nonvolatile substances arises or not depends on the kind of nonvolatile substances and the total amount (namely, the concentration of nonvolatile substances and the flow rate of the sample solution) introduced into the ion source. For example, when substances are analyzed at a flow rate of 1 micro liter per minute continuously for several hours using a phosphoric acid buffer having a concentration of 10 millimol/liter, the ion intensity observed by the mass spectrometer may reduce.

[0016] Even in the apparatus using the conventional electrospray method shown in Fig. 10, the outer periphery of a jet is sprayed toward the ion introduction aperture, so that a part of droplets generated by spray reaches in the neighborhood of the ion introduction aperture. Therefore, when a sample solution containing nonvolatile compounds of high concentration is introduced into the ion source, there is a possibility that the ion introduction aperture clogs up with nonvolatile compounds salted out by vaporization of droplets. Therefore, in the same way as with an apparatus using the atmospheric pressure chemical ionization method shown in Fig. 9, a problem arises that if the analysis is continued for many hours, the aperture clogs up and ions cannot be fetched by the mass spectrometric portion.

[0017] For the aforementioned reason, an apparatus having an ion source for allowing stable analysis for many hours even if a solution containing nonvolatile compounds of high concentration is introduced is required.

[0018] From US-A-4,209,696 the features of the first parts of claims 1 and 15 are known. This document discloses a mass spectrometric apparatus for mass anal-

ysis of molecular con-stituents of liquid wherein in the first ionisation step an electro-spray technique produces charged droplets and in the second ionisation step an electron gun causes ionisation of gaseous molecules of said charged droplets. Both ionisation steps are carried out under high vacuum.

SUMMARY OF THE INVENTION

[0019] An object of present invention is to enable an analysis of a sample solution containing non-volatile compounds.

[0020] This object is met by an apparatus according to claim 1 and a method according to claim 15. Preferred embodiments are disclosed in the dependent claims.

[0021] According to an embodiment of the present invention, the following steps are carried out : Introducing a sample solution containing nonvolatile compounds sent to the ion source into the metallic tube, spraying the sample solution by electrospray at a high voltage applied between the metallic tube and the electrode externally installed, ionizing gaseous sample molecules obtained by vaporizing obtained droplets by chemical reaction, and analyzing ions of sample molecules by the MS.

[0022] Namely, the present invention is characterized in the method and constitution that nonvolatile compounds contained in a sample solution are ionized by the first ionization means and removed by the electric field, and then a substance contained in the sample solution to be analyzed is ionized by the second ionization means, and ions of the target substance are analyzed by the spectrometric portion.

[0023] Since a sample solution sent to the ion source is sprayed by electrospray, no nonvolatile compounds will be salted out by vaporization of solvent molecules and the metallic tube can be prevented from clogging.

[0024] Electrospray is a method for collecting ions in a solution on the liquid surface by the electric field and crushing the solution by the force of repulsion acting between ions so as to generate fine charged droplets. When charged droplets obtained by electrospray are vaporized, ions existing in the solution can be fetched in the gas phase. Therefore, some of nonvolatile compounds which exist in the solution as ions can be converted to gaseous ions by electrospray. Ions generated by electrospray are drifted by the electric field between the metallic tube and the metallic block constituting the vaporization portion and captured by the metallic block or the trajectory thereof is curved by the potential applied to the needle electrode installed in the ionization portion, so that they cannot reach the ion introduction aperture. Therefore, no nonvolatile compounds will salt out around the ion introduction aperture and the aperture will not be clogged out.

[0025] A substance to be analyzed which is not ionized in the solution is not converted to gaseous ions by electrospray but diffused in the atmosphere as gaseous molecules which are electrically neutral and reaches the ionization portion. In the ionization portion, ions of the substance to be analyzed are generated by a corona discharge generated by the needle electrode and chemical ionization reaction caused by it. Ions of the substance to be analyzed are fetched and analyzed by the mass spectrometric portion in a vacuum via the ion introduction aperture.

[0026] A nonvolatile salt which is represented by sodium phosphate is dissociated in a solvent such as water and exists as ions. Therefore, the LC/MS of the present invention can use a mobile phase containing a nonvolatile salt which is represented by a phosphoric acid buffer though it is conventionally difficult to use for many hours.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027]

Fig. 1 is a schematic view showing the constitution of a mass spectrometric apparatus using an electrospray method as a first ionization means and a chemical ionization method as a second ionization means which is an embodiment of the present invention;

Fig. 2 is an illustration for explaining the embodiment shown in Fig. 1 in detail;

Fig. 3 is a schematic sectional view showing an embodiment in which the end of the metallic tube is placed in the volatilization portion and a sample solution is directly sprayed toward the metallic block;

Fig. 4 is a schematic sectional view showing an embodiment in which a shielding plate for preventing large droplets from splashing and reaching the ionization portion is installed;

Fig. 5 is a schematic sectional view showing an embodiment in which irradiation of infrared light is used as a vaporization method of the vaporization portion;

Fig. 6 is a schematic sectional view showing an embodiment in which a sample solution is sprayed perpendicularly to the center axis of the ion introduction aperture;

Fig. 7 is a schematic sectional view showing an embodiment in which a pan for collecting droplets is used;

Fig. 8 is a schematic sectional view showing an embodiment in which a gas spray ionization method is used as a first ionization means;

Fig. 9 is a schematic view showing the constitution of a liquid chromatograph - mass spectrometer using the conventional atmospheric pressure chemical ionization method;

Fig. 10 is a schematic sectional view showing the constitution of a liquid chromatograph - mass spectrometer using the conventional electrospray method;

Fig. 11 is a graph showing a change with time of the ion intensity obtained by a mass spectrometer using the conventional atmospheric pressure chemical ionization method; and

Fig. 12 is a graph showing a change with time of the ion intensity obtained by the mass spectrometer of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0028] Fig. 1 is a schematic view showing the constitution of the mass spectrometric apparatus of the present invention. A sample separated by a liquid chromatograph 14 is sprayed by an electrospray portion 15 together with the mobile phase. Droplets obtained by spray are promoted in vaporization in a vaporization portion 5. Gaseous sample molecules generated by the vaporization portion 5 are ionized by chemical reaction in an ionization portion 6. Ions of the sample generated by the ionization portion 6 are introduced into an ion introduction aperture 9b and a high vacuum portion 12 which is exhausted by an exhaust system 10b via an ion introduction aperture 9a and a differential pumping portion 11 which is exhausted by an exhaust system 10a.

[0029] Ions introduced into a vacuum are analyzed in mass by a mass spectrometric portion 13. The ionization portion 6 may be installed in the differential pumping portion 11. The differential pumping portion 11 has a pressure between several Pascal to several hundreds Pascal and can generate ions by chemical reaction because sample molecules and reaction gas collide with each other.

[0030] Fig. 2 is a drawing showing a more detailed structure than the constitution shown in Fig. 1. The liquid chromatograph 14 comprises a mobile phase reservoir 50, a pump 51, a sample introduction portion 52, a separation column 53, and a pipe 1. A mobile phase in the mobile phase reservoir 50 is pumped up by the pump 51 and sent to the sample introduction portion 52 and the separation column 53 at the predetermined flow rate via the pipe 1. The sample is introduced from the sample introduction portion 52 and sent to the separation column 53 together with the mobile phase. The separation column 53 is filled up with a packing material. The sample is separated by interaction with the packing material. The sample solution eluted from the separation column 53 is introduced into the metallic tube 3 via the pipe 1 and the connector 2. When a high voltage is applied between the metallic tube 3 and the metallic block 4b by using a high voltage source 8b, charges with the same sign are accumulated on the surface of the solution by the electric field in the neighborhood of the end of the metallic tube 3. When the electrostatic repulsion force generated by the accumulated charges becomes stronger than the surface tension of the solution, so-called electrospray for generating many fine charged droplets is caused. Fine droplets generated by spray are introduced into the vaporization portion 5 comprising the heated metallic block 4b. The metallic block 4b is heated at about 300°C by a heater (not shown in the drawing). Droplets generated by spray are vaporized by heat while they are passing through the aperture of the metallic block 4b.

[0031] Sample molecules vaporized in the vaporization portion 5 are introduced into the ionization portion 6. The needle electrode 7 is installed in the ionization portion 6. When a high voltage is applied to this needle electrode 7 by using the high voltage source 8a, a corona discharge is generated in the ionization portion 6. When gaseous sample molecules obtained by volatilization of droplets reach the corona discharge portion, a chemical reaction with primary ions such as hydronium ions generated by the corona discharge is caused and ionization of sample molecules is realized.

[0032] In this case, since the sample solution is sprayed by electrospray, nonvolatile compounds will not be salted out by vaporization of solvent molecules and the metallic tube 3 can be prevented from clogging up. The part of the nonvolatile compounds in the solution which is ionized is converted to gaseous ions by electrospray. These ions are captured by the metallic block 4b constituting the vaporization portion 5 or the trajectory thereof is curved by the potential applied to the needle electrode 7 installed in the ionization portion 6, so that they cannot reach the ion introduction aperture 9a. Therefore, even if a sample solution containing nonvolatile compounds is used, the nonvolatile compounds will not salt out around the ion introduction aperture 9a and there is no possibility that the ion introduction aperture 9a is clogged up.

[0033] Therefore, according to the present invention, even if a sample solution containing nonvolatile compounds of high concentration is introduced, an ion source for generating ions of a substance to be analyzed stably for many hours can be realized. Furthermore, according to the present invention, a mass spectrometric apparatus for analyzing a sample solution containing nonvolatile compounds of high concentration stably for many hours can be realized.

[0034] The polarity (positive or negative) of voltages to be applied to the needle electrode 7 and the metallic tube 3 by the high voltage sources 8a and 8b may be switched independently of each other according to the property of a substance to be analyzed and the property of nonvolatile compounds in the sample solution. For example, when a substance to be analyzed has a strong proton affinity and is apt to be converted to protonated ions, it is desirable to apply a positive voltage to the needle electrode 7. When a substance to be analyzed has a property that negative ions which are deprotonated are easily generated, it is desirable to apply a negative voltage to the needle electrode 7.

[0035] Next, the effect of the present invention described in Fig. 2 will be explained on the basis of the experimental results. A 50% methanol water solution

containing sodium dihydrogenphosphate having a concentration of 20 millimol/liter is used as a mobile phase and fed to the ion source by an LC pump at a flow rate of 50 micro liter per minute. β-hydroxytheophylline(concentration 100 ppm) is used as a sample. This sample is introduced from an LC sample injector in units of 2 micro liters each time by taking time. The mass spectrometer monitors protonated molecular ions (molecular weight 225) of β-hydroxytheophylline.

[0036] Fig. 11 shows a change with time of the ion intensity observed by an apparatus using the conventional atmospheric pressure chemical ionization method. The ion intensity starts reduction about 30 minutes after start of analysis. When the apparatus is disassembled and examined, it is found that the cause of reduction of the ion intensity is that a nonvolatile salt (sodium phosphate) in the mobile phase salts out in the neighborhood of the ion introduction aperture and the ion introduction aperture is clogged up.

[0037] Fig. 12 shows a change with time of the ion intensity measured by using the apparatus of the present invention shown in Fig. 2. The dotted line shown in the drawing indicates the mean level of the maximum values of the ion intensity when each sample is introduced and almost the same intensity is obtained over a period of 6 hours. As shown in Fig. 12, according to the present invention, even if a mobile phase containing a nonvolatile salt is introduced into the ion source, a reduction in the ion intensity caused by clogging of the metallic tube or ion introduction aperture is not seen and ions are observed stably for many hours.

[0038] As shown in Fig. 11, if a mobile phase containing a nonvolatile salt is used in the conventional LC/MS under the aforementioned condition, a cleaning operation for the aperture and others is required every analysis for about 30 minutes. To clean the aperture, it is necessary to stop the exhaust system and disassemble the apparatus. To restart analysis, it requires about 2 hours including the time of reexhaust after completion of cleaning, so that the operability as an analytical apparatus is extremely bad. Furthermore, when the vacuum pump starts exhausting from the atmospheric pressure to a vacuum, it is applied with a great load, so that repetition of stopping and reexhausting the exhaust system is a factor for shortening the life time of the vacuum pump. Furthermore, when the apparatus is disassembled and assembled again, the analytical conditions are changed by a shift in installation position of each part constituting the ion source and a change in temperature of the heating part, and the reproducibility of the ion intensity observed by the mass spectrometer is bad, and the accuracy of quantitative analysis of a substance to be analyzed gets worse. In the conventional apparatus, it is necessary to end one analysis including adjustment of the ion source for 30 minutes during which ions are observed stably. However, a time of 30 minutes is not always sufficient for use of the separation ability of the LC at its maximum. For example, there is a method available for changing the composition of a mobile phase with time and eluting a substance to be analyzed. However, if the composition is changed in a short time, no sufficient separation may be obtained. The cause thereof is considered to be that if the composition of the mobile phase is changed too fast, the packing material in the separation column and the mobile phase cannot be kept in the equilibrium state.

[0039] The apparatus of the present invention can be used continuously for about 10 hours even if a mobile phase containing a nonvolatile salt which is conventionally difficult to use is used. If an operator cleans and adjusts the apparatus before starting operation every morning, he can obtain data during his operation in a day. Therefore, the apparatus of the present invention has advantages that the operability is remarkably improved compared with a conventional apparatus, and the burden imposed on the vacuum pump is lightened, and the life time of the vacuum pump can be lengthened. The apparatus of the present invention is characterized in that since it can repeat measurement under the same analytical condition, the accuracy of quantitative analysis is high and a sufficient time can be put in separation, so that analysis by the LC/MS fully utilizing the separation ability of the LC is possible.

[0040] Whether a problem that ions cannot be observed stably due to clogging of the metallic tube or aperture arises or not depends on the kind of nonvolatile substances and the total amount (namely, the concentration of nonvolatile substances and the flow rate of the solution) sent to the ion source.

[0041] For example, there is a capillary electrophorsis method (hereinafter abbreviated to CE) available as a separation means different from the LC. This is a method for separating a sample by electrophorsis using a fused-silica capillary of several tens microns in inner diameter. A buffer solution containing a nonvolatile salt having a concentration of several tens millimol/liter may be used as a separation medium of CE. A flow of a buffer solution which is called an electroosmosis flow is generated due to dissociation of the inner wall of the capillary, though the rate of electroosmosis flow is generally low such as 0.1 micro liter per minute or less. Therefore, in a so-called CE/MS using an MS as a CE detector, a problem of clogging of the aperture will not arise.

[0042] When the flow rate of a solution sent from the LC is high and it is difficult to continue electrospray stably, as shown in Fig. 2, a splitter 16 may be installed so as to introduce a part of the solution into the metallic tube 3. Also as shown in Fig. 2, a spray gas 17 may flow from the outside of the metallic tube 3 so as to assist the electrospray.

[0043] When a narrow separation column with an inner diameter of from several tens microns to several hundreds microns which is called a capillary column is used in the LC, it may be difficult to continue the electrospray stably because the flow rate of a solution sent from the LC is low. It may be also difficult to continue the

electrospray stably because the viscosity or electric conductivity of the solution is excessively high depending on the concentration of the solute. If this occurs, also shown in Fig. 2, it is possible to provide an area for flowing an auxiliary spray solution 18 around the metallic tube 3 and mix it with a solution sent from the LC in the neighborhood of the end of the metallic tube 3 so as to set the flow rate, viscosity, and electric conductivity to the conditions for continuing the electrospray stably.

[0044] As shown in Fig. 3, the end of the metallic tube 3 may be placed in the vaporization portion 5. Also as shown in Fig. 3, a solution may be sprayed directly toward the metallic block 4b. A sample solution is subjected to first ionization, that is, electrospray at a high voltage applied between the metallic tube 3 and the metallic block 4b by the high voltage source 8b. The metallic tube 3 and the metallic block 4b are insulated from each other by an insulating tube 19. Droplets sprayed to the metallic block 4b which is heated to a temperature higher than the boiling point of the solution are vaporized instantaneously and gaseous sample molecules are obtained. When sample molecules reach the corona discharge portion, they are chemically reacted with primary ions such as hydronium ions generated by corona discharge and ionization of sample molecules is realized by second ionization, that is, chemical ionization. Ions of sample molecules are fetched by the high vacuum portion 12 which is exhausted to about 10-3 Pa by the exhaust system 10b via the differential pumping portion 11 which is exhausted to from several tens Pa to several hundreds Pa by the ion introduction aperture 9a and the exhaust system 10a and the mass thereof is analyzed by the mass spectrometric portion 13.

[0045] To increase the arrival efficiency of sample molecules to the ionization portion, as shown in Fig. 3, it is possible to provide an inclined wall inside the metallic block 4b,(10) electrostatically spray sample molecules toward the inclined wall in the oblique direction, and (10) flow a gas 20 such as nitrogen gas toward the ionization portion. It is desirable to preheat the gas 20 at a temperature higher than the room temperature.

[0046] When large droplets are generated by electrospray in an apparatus having the constitution shown in Fig. 2, they cannot be vaporized perfectly in the vaporization portion 5 by the heated metallic block 4b and may reach the ionization portion 6 where a corona discharge is generated by the needle electrode 7 as they are. When droplets reach the portion where a corona is generated, there is a possibility that they short-circuit the needle electrode 7 and the ion introduction aperture 9a and the high voltage source 8a or others may be damaged.

[0047] To prevent it, as shown in Fig. 4, it is possible to arrange an electrode 21a so as to shield the ionization portion 6 where a corona discharge is generated by the end of the metallic tube 3 and the needle electrode 7 and electrostatically spray droplets toward the electrode 21a. In this case, to increase the vaporization efficiency of droplets, it is desirable to heat the electrode 21a by a heater 22a beforehand. In an apparatus having the constitution shown in Fig. 4, gaseous molecules are transported and ionized in the ionization portion 6, so that a short-circuit due to droplets adhered to the needle electrode 7 can be avoided. In Fig. 4, the shape of the electrode 21a may be not only laminar but also meshed. To increase the arrival efficiency of sample molecules to the ionization portion 6, it is possible to flow a gas 20 toward the ionization portion 6 as shown in Fig. 3.

[0048] In the embodiments shown in Figs. 2 to 4, a constitution in which a heated metallic block is used as a means for vaporizing droplets is shown. However, a method for irradiating infrared light may be used for vaporization of droplets.

[0049] Fig. 5 shows an embodiment using irradiation of infrared light as a vaporization means. A sample solution is electrostatically sprayed at a voltage applied between the metallic tube 3 and a mesh 23a. It is desirable that the mesh 23a is heated beforehand. Droplets obtained by spray are sent to the vaporization portion 5. Infrared light emitted from a heater 22b connected to a power source 24 is irradiated to droplets in the vaporization portion 5 so as to vaporize them. When the heater 22b is degraded because droplets collide directly with it, it is possible to install a glass tube 25 inside the heater 22b so as to protect it. To increase the vaporization efficiency of droplets, it is desirable to remove water vapor in the spray gas 17 beforehand. It is also desirable to heat the spray gas 17 at the room temperature or higher beforehand. Gaseous sample molecules obtained in the vaporization portion 5 are ionized in the ionization portion 6.

[0050] In an apparatus having the constitution shown in Figs. 2 to 5, a sample solution containing nonvolatile compounds can be used in the LC/MS. However, when a sample solution containing nonvolatile compounds of an extremely high concentration is introduced into the ion source or the analysis requires more hours, it is possible to change the spray direction of the sample solution to a direction different from the arrangement direction of the ion introduction aperture. Fig. 6 shows an example in which a sample solution is sprayed perpendicularly to the center axis of the ion introduction aperture 9a. The sample solution introduced into the metallic tube 3 is sprayed toward an opposite electrode 21b. It is desirable that the electrode 21b is heated at a temperature higher than the boiling point of the solution beforehand.

[0051] Nonvolatile compounds are salted out on the electrode 21b. Volatile sample molecules are vaporized and introduced into the ionization portion 6 via the heated metallic block 4b. To increase the arrival efficiency of sample molecules to the ionization portion 6, it is possible to install a gas feed port 26 and flow a gas 20 such as dry nitrogen gas toward the ionization portion 6. It is desirable to heat the gas 20 beforehand. It is possible that by installing an exhaust port 27 and exhausting gas outside from the exhaust port, a gas flow is generated

toward the ionization portion 6 from the portion where the solution is sprayed and sample molecules are introduced efficiently into the ionization portion 6.

[0052] In Fig. 6, the electrospray method is described as a method for spraying a solution. However, to change the spray direction of a sample solution to a direction different from the arrangement direction of the ion introduction aperture, it is possible to use a spray method other than electrospray, for example, heating spray or ultrasonic spray. When a substance to be analyzed is volatile, it is heated, vaporized, and diffused on the electrode 21b and reaches the ionization portion 6.

[0053] In an apparatus having the constitution shown in Fig. 6, nonvolatile compounds salt out on the electrode 21b. Therefore, by removing and cleaning only this electrode 21b, it can be maintained easily.

[0054] Fig. 7 is a drawing showing a constitution in which a solution is sprayed toward a mesh 23b in place of the opposite electrode 21b shown in Fig. 6. It is desirable to heat the mesh 23b beforehand. A pan 28 can be installed behind the mesh 23b and maintained simply by exchanging. Furthermore, a solution collected in the pan 28 is sampled and an analytical means other than the mass spectrometry, for example, an analytical method using fluorescence or emission or an immunological analytical method may be executed for it.

[0055] The present invention is characterized in that nonvolatile compounds in a solution are ionized by the first ionization means and then removed by the electric field and a substance to be analyzed which is not ionized by the first ionization means is ionized by the second ionization means and analyzed. Therefore, if nonvolatile compounds can be ionized, the first ionization means may not be the electrospray method. Fig. 8 shows an embodiment in which the gas spray ionization method is used as a first ionization means.

[0056] A sample solution is introduced into a capillary 61 via the pipe 1 and the connector 2. The capillary 61 may be a metallic tube or an insulating tube. A spray gas introduction tube 62 is arranged around the capillary 61 and the spray gas 17 flows in it. When the spray gas 17 increases its speed, the solution is crushed to pieces and fine droplets are generated. In the droplets obtained by doing this, nonvolatile compounds which exist in the solution as ions are fetched. When the solvent is evaporated from the droplets, gaseous ions of the nonvolatile compounds are generated. The trajectory of the gaseous ions is curved by the potential applied to the needle electrode 7 installed in the ionization portion 6, so that the ions cannot reach the ion introduction aperture 9a. As a result, the nonvolatile compounds do not salt out in the neighborhood of the ion introduction aperture 9a and the ion introduction aperture 9a is not clogged up. A substance to be analyzed which is electrically neutral reaches the ionization portion 6 by diffusion in the same way as with the embodiment shown in Fig. 2 and is ionized and analyzed. To promote vaporization of droplets, the vaporization portion 5 comprising the heated metallic block 4b may be installed. Droplets are vaporized by heat while they are passing through the aperture of the metallic block 4b. To increase the efficiency for removing ions of nonvolatile compounds, it is possible to generate an electric field between the spray gas introduction tube 62 and the metallic block 4b by the high voltage source 8c. Ions of nonvolatile compounds are drifted by the electric field in the direction of the metallic block 4b or the spray gas introduction tube 62 according to the ion polarity and captured by the metallic block 4b or the spray gas introduction tube 62.

[0057] As shown by the above description, according to the present invention, even if a solution containing nonvolatile compounds of high concentration is introduced into the ion source, the capillary for spraying the solution and the aperture for fetching ions generated under the atmospheric pressure into a vacuum can be prevented from clogging up. As a result, a substance to be analyzed in the solution can be ionized stably for many hours and the ions can be introduced and analyzed in the spectrometric portion arranged in a vacuum. Therefore, a sample obtained from a living matter or environment can be analyzed without a complicated pretreatment being executed. Furthermore, a mobile phase containing a nonvolatile salt which cannot be used for many hours in a conventional LC/MS can be used, so that analysis by the LC/MS fully utilizing the separation ability of the LC is possible.

[0058] Main symbols used in the drawings mentioned above are shown below in a batch.

1: Pipe, 2: Connector, 3: Metallic tube, 4a, 4b: Metallic blocks, 5:Vaporization portion, 6: Ionization portion, 7: Needle electrode, 8a, 8b, 8c: High voltage sources, 9a, 9b: Ion introduction apertures: 10a, 10b: Exhaust systems, 11: Differential pumping portion, 12: High vacuum portion, 13: Mass spectrometric portion, 14: Liquid chromatograph, 15: Electrospray portion, 16: Splitter, 17: Spray gas, 18: Auxiliary spray solution, 19: Insulating tube, 20: Gas, 21a, 21b, 21c: Electrodes, 22a, 22b: Heaters, 23a, 23b: Meshes, 24: Power source, 25: Glass tube, 26: Gas feed port, 27: Exhaust port, 28: Pan, 30: Power source, 31: Deflection electrode, 32: Capture plate, 40: Spray gas outlet, 41: Shielding plate, 50: Mobile phase reservoir, 51: Pump, 52: Sample introduction portion, 53: Separation column, 60: Gas spray ion generation port, 61: Capillary, 62: Spray gas introduction tube.

Claims

1. A mass spectrometric apparatus comprising

supplying means (14) for supplying a sample solution in-cluding a solvent and a solute to an outlet;

first ionisation means (15; 60) for receiving the sample solution from the outlet and spraying the received sample solution, thereby ionising at least a

portion of the received sample solution;

second ionisation means (6) for receiving at least a portion of the sprayed sample solution produced by the first ionisation means and ionising at least a portion of the received sprayed sample solution, thereby producing ions; and

analysing means (13) for receiving at least some of the ions produced by the second ionisation means and analysing masses of the received ions;

characterised in that

said second ionisation means (6) is capable to cause the received sprayed sample solution to perform a chemical reaction at atmospheric pressure or substantially atmospheric pressure, thereby producing said ions.

2. The mass spectrometric apparatus according to claim 1, wherein said second ionisation means (6) comprises an electrode (7) for generating an electric field to eliminate at least a portion of the ions produced by the first ionisation means (15).

3. The mass spectrometric apparatus according to claim 2, wherein said electrode (7) is a needle electrode producing a corona discharge.

4. The mass spectrometric apparatus according to any of claims 1 to 3, wherein the first ionisation means (15; 60) is located at atmospheric pressure or substantially atmospheric pressure, and wherein the analysing means (30) includes an analysing chamber (12) having an aperture (9) for receiving at least some of the ions, the analysing chamber analysing masses of the received ions.

5. The mass spectrometric apparatus according to any of claims 1 to 4, wherein said first ionisation means (15; 60) is capable to gas-spray or electrospray the received sample solution, thereby ionising at least a portion of the received sample solution.

6. The mass spectrometric apparatus according to any of claims 1 to 5, wherein the supplying means (14) comprises means (16) for keeping the sample solution at a predetermined flow rate.

7. The mass spectrometric apparatus according to any of claims 1 to 6, wherein the supplying means (14) comprises means (53) for separating substance in said sample solution by components.

8. The mass spectrometric apparatus according to any of claims 1 to 7, further comprising vaporisation means (5) provided between said first and second ionisation means (15; 60; 6) for vaporising the sample solution sprayed by said first ionisation means.

9. The mass spectrometric apparatus according to claim 8, wherein said vaporisation means (5) comprises a heated metallic block (4b) which includes an aperture in which the sprayed sample solution is vaporised by heat while passing therethrough.

10. The mass spectrometric apparatus according to claims 8 or 9, further comprising a high voltage source (8) for applying a high voltage between the first ionisation means (15; 60) and the vaporising means (5).

11. The mass spectrometric apparatus according to claim 9, wherein said first ionisation means (15) includes a metallic tube (3) for electro-spraying the sample solution which is arranged in said heated metallic block (4b) of said vaporisation means (5).

12. The mass spectrometric apparatus according to claim 10, wherein said metallic tube (3) is provided in an angular manner with respect to an aperture of the heated metallic block (4b), and wherein gas is introduced in said metallic block to flow the sprayed sample solution to the second ionisation means (6).

13. The mass spectrometric apparatus according to claim 11, comprising a laminar or meshed electrode (28) which is located behind the metallic tube (3) and is preferably heated.

14. The mass spectrometric apparatus according to any of claims 1 to 13, comprising an electrode (21b) or a mesh (23b) onto which the sample solution is sprayed by said first ionisation means (15).

15. An analytical method comprising the steps of

preparing a sample solution including a solvent and a solute;

spraying the sample solution by first ionisation means (15; 60) thereby ionising at least a portion of the sample solution;

ionising at least a portion of the sprayed sample solution by second ionisation means (6) thereby producing ions; and

receiving through an aperture of an analysing chamber at least some of the ions produced by the second ionisation means and analysing masses of the received ions;

characterised in that

said ionising step performed by the second ionisation means (6) includes a step of causing the sprayed sample solution to perform a chemical reaction at atmospheric pressure or substantially atmospheric pressure, thereby producing said ions.

16. The method according to claim 15, wherein said ionising step performed by the second ionisation means (6) includes a further step of generating an

electric field to eliminate at least a portion of the ions produced by the first ionisation means (15).

17. The method according to claims 15 or 16, wherein said spraying step performed by the first ionisation means (15; 60) includes a step of electro-spraying or gas-spraying the sample solution at atmospheric pressure or substantially atmospheric pressure, thereby ionising the portion of the sample solution.

18. The method according to any of claims 15 to 17, further comprising a step of separating the prepared sample solution into components.

Patentansprüche

1. Massenspektrometer mit

einer Zuführeinrichtung (14) zum Zuführen einer ein Lösungsmittel und Gelöstes enthaltenden Probenlösung an einen Auslaß;

einer ersten Ionisiereinrichtung (15; 60) zum Aufnehmen der Probenlösung aus dem Auslaß und Zerstäuben der aufgenommenen Probenlösung, wobei wenigstens einen Teil der aufgenommenen Probenlösung ionisiert wird;

einer zweiten Ionisiereinrichtung (6) zum Aufnehmen wenigstens eines Teils der durch die erste Ionisiereinrichtung erzeugten zerstäubten Probenlösung, und zum Ionisieren wenigstens eines Teils der aufgenommenen zerstäubten Probenlösung, wobei Ionen entstehen; und

einer Analyseeinrichtung (13) zum Aufnehmen wenigstens einiger der durch die zweite Ionisiereinrichtung erzeugten Ionen und Analysieren der Masse der aufgenommenen Ionen;

dadurch gekennzeichnet, daß die zweite Ionisiereinrichtung (6) bewirkt, daß die aufgenommene zerstäubte Probelösung eine chemische Reaktion bei Atmosphärendruck oder im wesentlichen bei Atmosphärendruck ausführt, um die Ionen zu erzeugen.

2. Massenspektrometer nach Anspruch 1, wobei die zweite Ionisiereinrichtung (6) eine Elektrode (7) zum Erzeugen eines elektrischen Feldes aufweist, um wenigstens einen Teil der durch die erste Ionisiereinrichtung (15) erzeugten Ionen zu beseitigen.

3. Massenspektrometer nach Anspruch 2, wobei die Elektrode (7) eine Nadelelektrode ist, die eine Glimmentladung erzeugt.

4. Massenspektrometer nach einem der Ansprüche 1 bis 3, wobei die erste Ionisiereinrichtung (15; 60) unter Atmosphärendruck oder im wesentlichen unter Atmosphärendruck steht, wobei die Analyseeinrichtung (30) eine Analysekammer (12) mit einer Öffnung (9) zum Aufnehmen wenigstens einiger der Ionen aufweist, und wobei die Analysekammer die Masse der aufgenommenen Ionen analysiert.

5. Massenspektrometer nach einem der Ansprüche 1 bis 4, wobei die erste Ionisiereinrichtung (15; 60) eine Gas- oder Elektro-Zerstäubung der aufgenommenen Probenlösung gestattet, um wenigstens einen Teil der aufgenommenen Probenlösung zu ionisieren.

6. Massenspektrometer nach einem der Ansprüche 1 bis 5, wobei die Zuführeinrichtung (40) eine Einrichtung (16) aufweist, die die Probenlösung auf einer vorbestimmten Durch-flußgeschwindigkeit hält.

7. Massenspektrometer nach einem der Ansprüche 1 bis 6, wobei die Zuführeinrichtung (14) eine Einrichtung (53) zum Zerlegen der Substanz in der Probenlösung in Komponenten aufweist.

8. Massenspektrometer nach einem der Ansprüche 1 bis 7, mit ferner einer zwischen der ersten und zweiten Ionisiereinrichtung (15; 60; 6) vorgesehenen Verdampfereinrichtung (5) zum Verdampfen der durch die erste Ionisiereinrichtung zerstäubten Probenlösung.

9. Massenspektrometer nach Anspruch 8, wobei die Verdampfereinrichtung (7) einen beheizten Metallblock (4b) mit einer Öffnung aufweist, in der die zerstäubte Probenlösung beim Durchströmen mittels Wärme zerstäubt wird.

10. Massenspektrometer nach Anspruch 8 oder 9, mit ferner einer Hochspannungsquelle (8) zum Anlegen einer Hochspannung zwischen der ersten Ionisiereinrichtung (15; 60) und der Verdampfereinrichtung (5).

11. Massenspektrometer nach Anspruch 9, wobei die erste Ionisiereinrichtung (50) ein in dem beheizten Metallblock (45) der Verdampfereinrichtung (5) angeordnetes Metallrohr (3) zum Elektro-Zerstäuben der Probenlösung aufweist.

12. Massenspektrometer nach Anspruch 10, wobei das Metallrohr (3) unter einem Winkel zu einer Öffnung des beheizten Metallblocks (4b) angeordnet ist, und wobei Gas in den Metallblock eingeführt wird, um eine Strömung der zerstäubten Probenlösung zur zweiten Ionisiereinrichtung (6) zu erzeugen.

13. Massenspektrometer nach Anspruch 12, mit einer hinter dem Metallrohr (3) angeordneten und vorzugsweise beheizten lamellen- oder gitterförmigen Elektrode (28).

14. Massenspektrometer nach einem der Ansprüche 1 bis 13, mit einer Elektrode (21b) oder einem Gitter (23b), auf die bzw. das die Probenlösung durch die erste Ionisiereinrichtung (15) zerstäubt wird.

15. Analyseverfahren, wobei
eine ein Lösungsmittel und Gelöstes enthaltende Probenlösung erzeugt wird,
die Probenlösung durch eine erste Ionisiereinrichtung (15; 60) zerstäubt wird, um wenigstens einen Teil davon zu ionisieren;
wenigstens ein Teil der zerstäubten Probenlösung durch eine zweite Ionisiereinrichtung (6) ionisiert wird, um Ionen zu erzeugen; und
wenigstens ein Teil der von der zweiten Ionisiereinrichtung erzeugten Ionen durch eine Öffnung der Analysekammer aufgenommen und die Masse der aufgenommenen Ionen analysiert wird;
dadurch gekennzeichnet, daß bei der durch die zweite Ionisiereinrichtung (6) ausgeführten Ionisierung bewirkt wird, daß die zerstäubte Probenlösung eine chemische Reaktion bei Atmosphärendruck oder im wesentlichen bei Atmosphärendruck ausführt, um Ionen zu erzeugen.

16. Verfahren nach Anspruch 15, wobei bei der durch die zweite Ionisiereinrichtung (6) ausgeführten Ionisierung ein elektrisches Feld erzeugt wird, um wenigstens einen Teil der durch die erste Ionisiereinrichtung (15) erzeugten Ionen zu beseitigen.

17. Verfahren nach Anspruch 15 oder 16, wobei beim Zerstäuben durch die erste Ionisiereinrichtung (15; 60) ein Elektro-Zerstäuben oder Gas-Zerstäuben der Probenlösung bei Atmosphärendruck oder im wesentlichen bei Atmosphärendruck erfolgt, um den Teil der Probenlösung zu ionisieren.

18. Verfahren nach einem der Ansprüche 15 bis 17, wobei die hergestellte Probenlösung in Komponenten zerlegt wird.

Revendications

1. Dispositif de spectrométrie de masse comportant
des moyens d'alimentation (14) pour alimenter une solution d'échantillon incluant un solvant et un soluté dans un orifice de sortie,
des premiers moyens d'ionisation (15 ; 60) pour recevoir la solution d'échantillon depuis l'orifice de sortie et pulvériser la solution d'échantillon reçue, en ionisant ainsi au moins une partie de la solution d'échantillon reçue,
des seconds moyens d'ionisation (6) pour recevoir au moins une partie de la solution d'échantillon pulvérisée produite par les premiers moyens d'ionisation et ioniser au moins une partie de la solution d'échantillon pulvérisée reçue, en produisant ainsi des ions, et
des moyens d'analyse (13) pour recevoir au moins certains des ions produits par les seconds moyens d'ionisation et analyser les masses des ions reçus,
caractérisé en ce que
lesdits seconds moyens d'ionisation (6) sont capables d'amener la solution d'échantillon pulvérisée reçue à effectuer une réaction chimique à une pression atmosphérique ou à une pression sensiblement atmosphérique, en produisant ainsi lesdits ions.

2. Dispositif de spectrométrie de masse selon la revendication 1, dans lequel lesdits seconds moyens d'ionisation (6) comportent une électrode (7) pour créer un champ électrique afin d'éliminer au moins une partie des ions produits par les premiers moyens d'ionisation (15).

3. Dispositif de spectrométrie de masse selon la revendication 2, dans lequel ladite électrode (7) est une électrode en forme d'aiguille produisant une décharge par effet corona.

4. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 3, dans lequel les premiers moyens d'ionisation (15 ; 60) sont à une pression atmosphérique ou à une pression sensiblement atmosphérique, et dans lequel les moyens d'analyse (30) incluent une chambre d'analyse (12) ayant une ouverture (9) pour recevoir au moins certains des ions, la chambre d'analyse analysant les masses des ions reçus.

5. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 4, dans lequel lesdits premiers moyens d'ionisation (15 ; 60) sont capables d'effectuer une pulvérisation gazeuse ou électrique de la solution d'échantillon reçue, en ionisant ainsi au moins une partie de la solution d'échantillon reçue.

6. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 5, dans lequel les moyens d'alimentation (14) comportent des moyens (16) pour maintenir la solution d'échantillon à un débit prédéterminé.

7. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 6, dans lequel les moyens d'alimentation (14) comportent des moyens (53) pour séparer en composants une substance de ladite solution d'échantillon.

8. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 7, comportant

de plus des moyens de vaporisation (5) agencés entre lesdits premiers et seconds moyens d'ionisation (15 ; 60 ; 6) afin de vaporiser la solution d'échantillon pulvérisée par lesdits premiers moyens d'ionisation.

9. Dispositif de spectrométrie de masse selon la revendication 8, dans lequel lesdits moyens de vaporisation (5) comportent un bloc métallique chauffé (4b) qui inclut une ouverture dans laquelle la solution d'échantillon pulvérisée est vaporisée sous l'action de la chaleur tout en passant à travers celle-ci.

10. Dispositif de spectrométrie de masse selon la revendication 8 ou 9, comportant de plus une source à haute tension (8) pour appliquer une haute tension entre les premiers moyens d'ionisation (15 ; 60) et les moyens de vaporisation (5).

11. Dispositif de spectrométrie de masse selon la revendication 9, dans lequel lesdits premiers moyens d'ionisation (15) incluent un tube métallique (3) pour effectuer une pulvérisation électrique de la solution d'échantillon qui est disposé dans ledit bloc métallique chauffé (4b) desdits moyens de vaporisation (5).

12. Dispositif de spectrométrie de masse selon la revendication 10, dans lequel ledit tube métallique (3) est agencé en formant un angle avec une ouverture du bloc métallique chauffé (4b), et dans lequel du gaz est introduit dans ledit bloc métallique pour faire s'écouler la solution d'échantillon pulvérisée dans les seconds moyens d'ionisation (6).

13. Dispositif de spectrométrie de masse selon la revendication 11, comportant une électrode lamellaire ou en treillis (28) qui est située derrière le tube métallique (3) et qui est de préférence chauffée.

14. Dispositif de spectrométrie de masse selon l'une quelconque des revendications 1 à 13, comportant une électrode (21b) ou un treillis (23b) sur lesquel la solution d'échantillon est pulvérisée par lesdits premiers moyens d'ionisation (15).

15. Procédé analytique comportant les étapes consistant à :

préparer une solution d'échantillon incluant un solvant et un soluté,

pulvériser la solution d'échantillon par des premiers moyens d'ionisation (15 ; 60) en ionisant ainsi au moins une partie de la solution d'échantillon,

ioniser au moins une partie de la solution d'échantillon pulvérisée par des seconds moyens d'ionisation (6) en produisant ainsi des ions, et

recevoir à travers une ouverture d'une chambre d'analyse au moins certains des ions produits par les seconds moyens d'ionisation et analyser les masses des ions reçus,

caractérisé en ce que

ladite étape d'ionisation effectuée par les seconds moyens d'ionisation (6) inclut une étape consistant à amener la solution d'échantillon pulvérisée à effectuer une réaction chimique à pression atmosphérique ou à une pression pratiquement atmosphérique, en produisant ainsi lesdits ions.

16. Procédé selon la revendication 15, dans lequel ladite étape d'ionisation effectuée par les seconds moyens d'ionisation (6) inclut une étape supplémentaire consistant à créer un champ électrique afin d'éliminer au moins une partie des ions produits par les premiers moyens d'ionisation (15).

17. Procédé selon les revendications 15 ou 16, dans lequel ladite étape de pulvérisation effectuée par les premiers moyens d'ionisation (15 ; 60) inclut une étape de pulvérisation électrique ou gazeuse de la solution d'échantillon à pression atmosphérique ou à une pression pratiquement atmosphérique, en ionisant ainsi la partie de la solution d'échantillon.

18. Procédé selon l'une quelconque des revendications 15 à 17, comportant de plus une étape consistant à séparer en composants la solution d'échantillon préparée.

FIG. 1

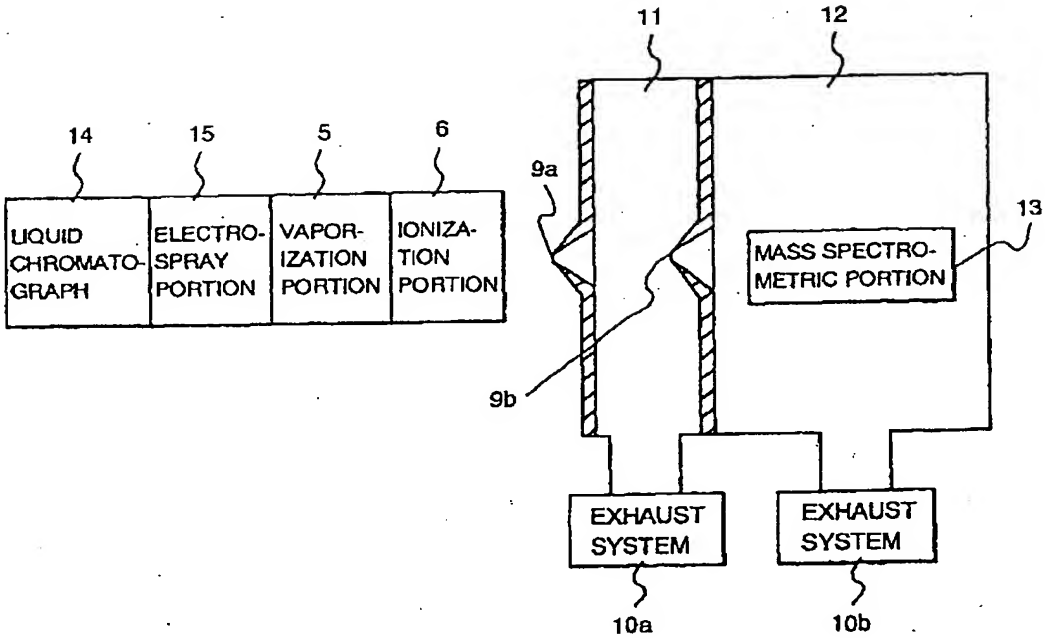

11
12
14
15
5
6
9a
13
LIQUID CHROMATO-GRAPH
ELECTRO-SPRAY PORTION
VAPOR-IZATION PORTION
IONIZA-TION PORTION
MASS SPECTRO-METRIC PORTION
9b
EXHAUST SYSTEM
EXHAUST SYSTEM
10a
10b

FIG. 2

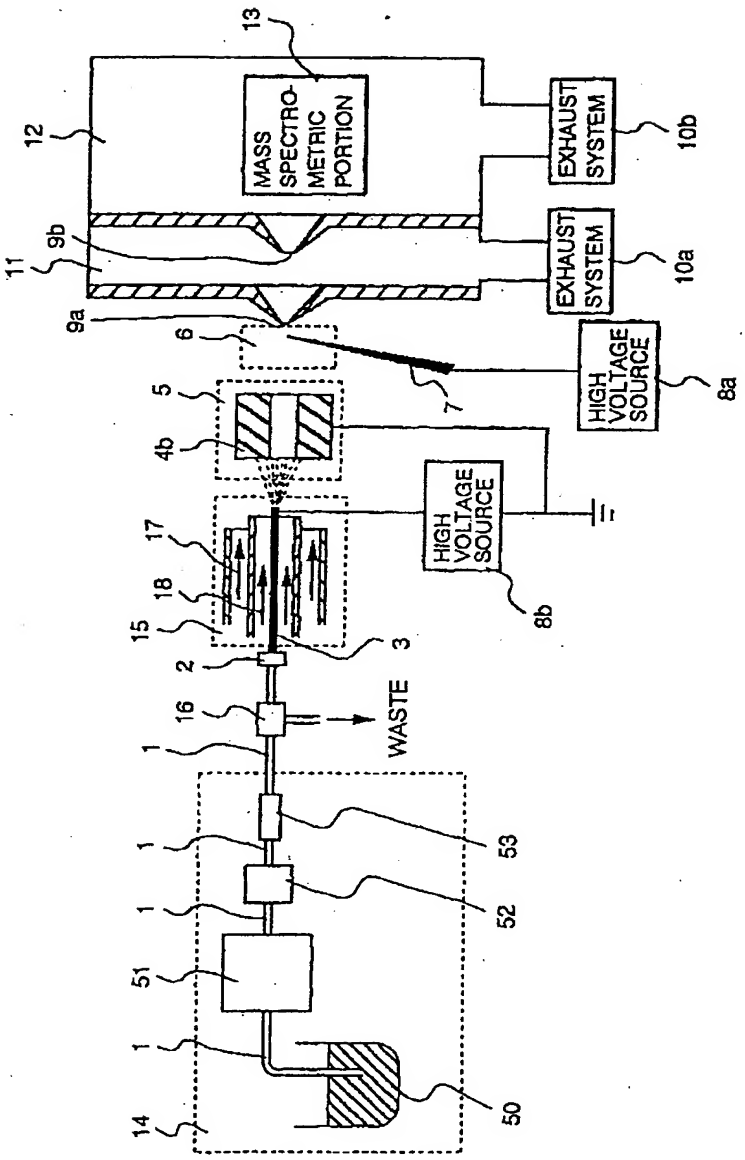

13
MASS SPECTRO-METRIC PORTION
12
EXHAUST SYSTEM
10b
9b
11
EXHAUST SYSTEM
10a
9a
6
HIGH VOLTAGE SOURCE
8a
7
5
4b
HIGH VOLTAGE SOURCE
8b
17
18
15
2
3
16
WASTE
1
53
52
51
50
14

FIG. 3

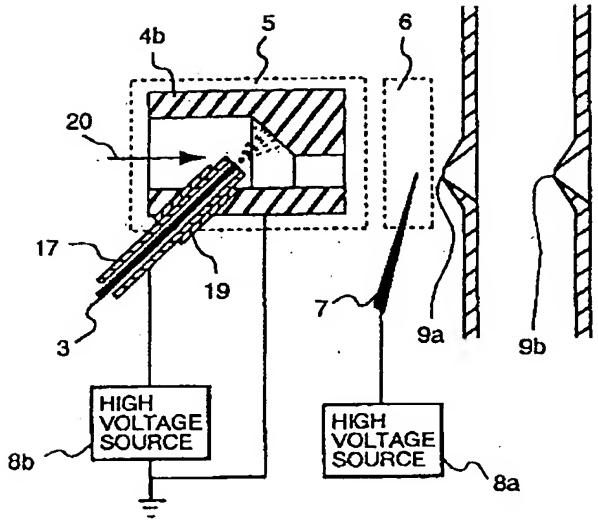

4b
5
6
20
17
19
3
7
9a
9b
HIGH VOLTAGE SOURCE
8b
HIGH VOLTAGE SOURCE
8a

FIG. 4

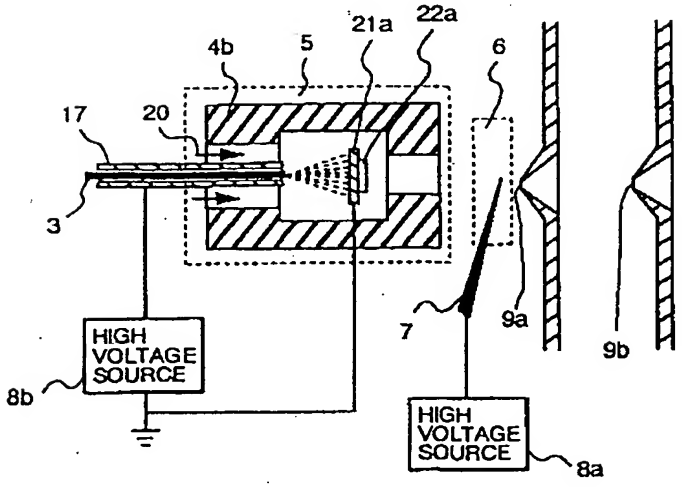

21a
22a
4b
5
6
17
20
3
7
9a
9b
HIGH VOLTAGE SOURCE
8b
HIGH VOLTAGE SOURCE
8a

FIG. 5

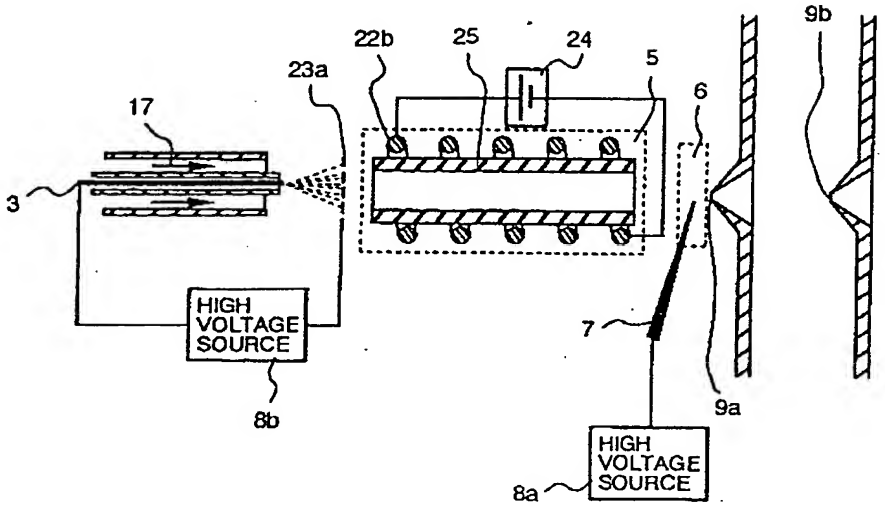

22b
25
24
23a
5
6
9b
17
3
HIGH VOLTAGE SOURCE
8b
7
9a
HIGH VOLTAGE SOURCE
8a

FIG. 6

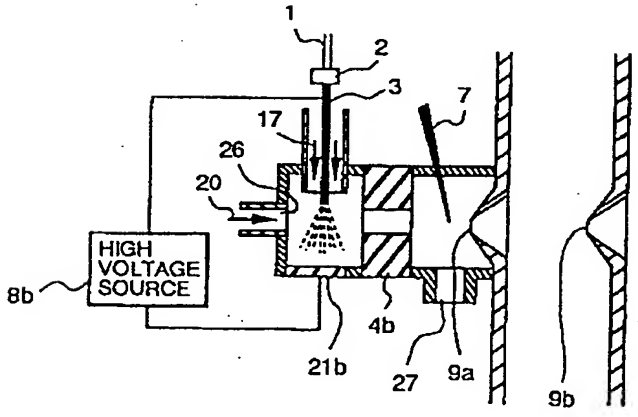

1
2
3
7
17
26
20
HIGH VOLTAGE SOURCE
8b
4b
21b
27
9a
9b

FIG. 7

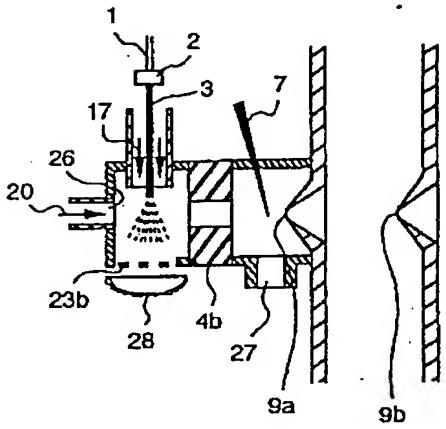

1
2
3
7
17
26
20
23b
28
4b
27
9a
9b

FIG. 8

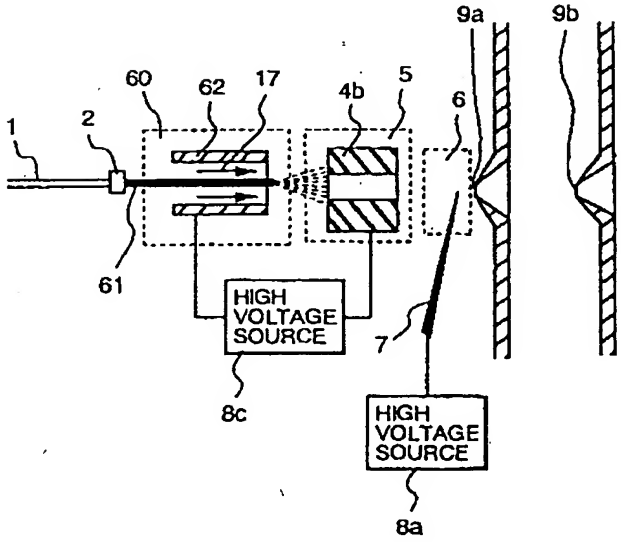

9a
9b
60
62
17
4b
5
6
1
2
61
HIGH VOLTAGE SOURCE
8c
7
HIGH VOLTAGE SOURCE
8a

FIG. 9

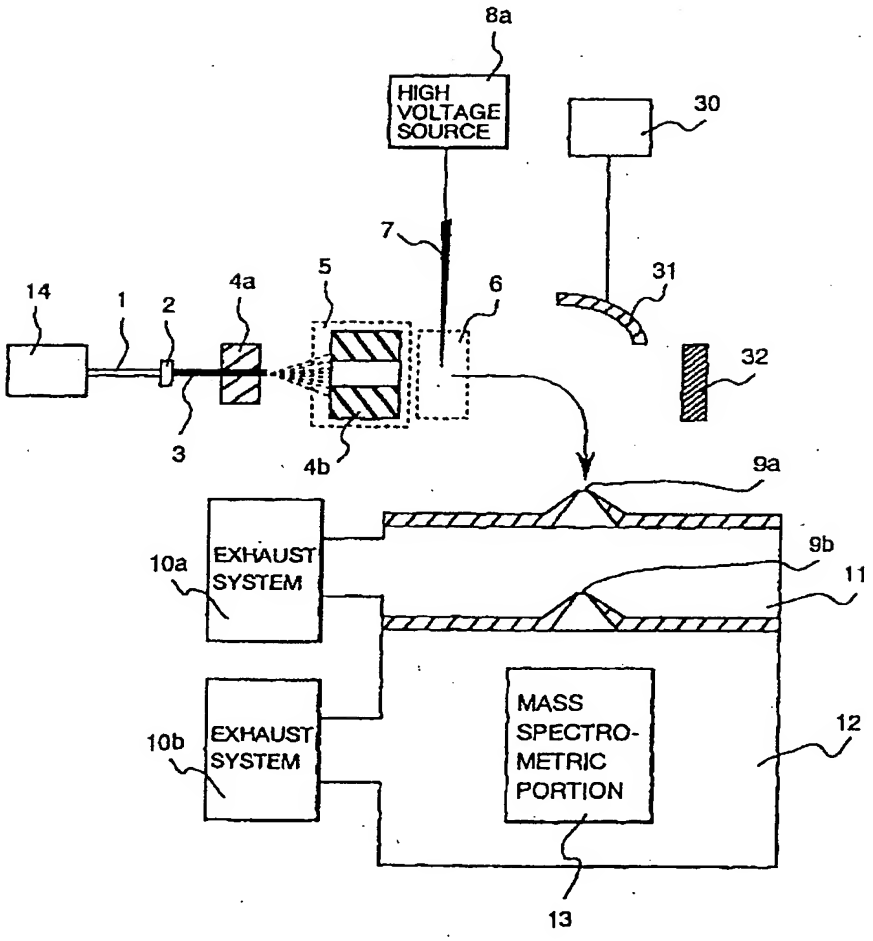

8a
HIGH VOLTAGE SOURCE
30
7
31
14
1
2
4a
5
6
32
3
4b
9a
9b
11
10a
EXHAUST SYSTEM
10b
EXHAUST SYSTEM
MASS SPECTRO-METRIC PORTION
12
13

FIG. 10

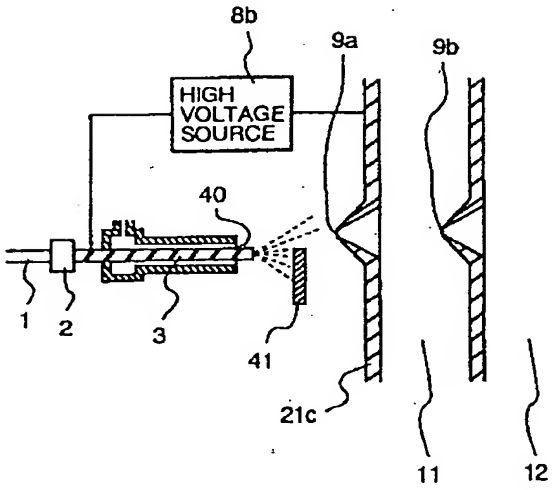


FIG. 11

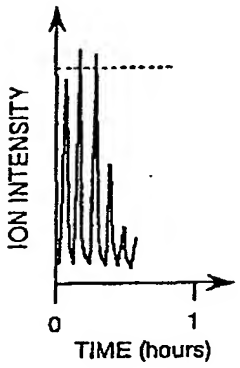
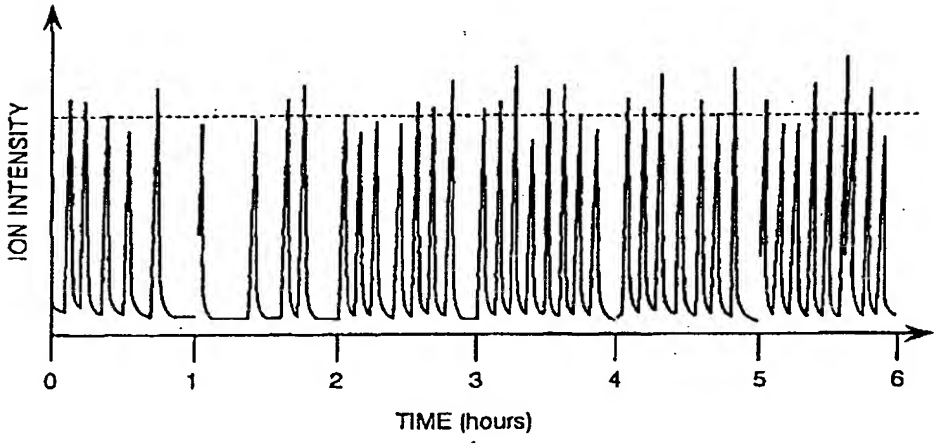

ION INTENSITY
0
1
TIME (hours)

FIG. 12


ION INTENSITY
0
1
2
3
4
5
6
TIME (hours)